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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/[illegible]558	/97	MERULLO	8105-009

HM12/0412

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EXAMINER	
ZEMAN,R	
ART UNIT	**PAPER NUMBER**
1645	4

DATE MAILED: 04/12/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/829,558	Merulo et al
Examiner	**Group Art Unit**
Robert A. Zeman	1645

☒ Responsive to communication(s) filed on *Apr 30, 1998* .

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-47* is/are pending in the application.

Of the above, claim(s) *11-17, 24-26, and 32-47* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-10, 18-23, and 27-31* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1645.

Claims 1-47 are pending in this application.

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-10, 18-23 and 27-31 in Paper No. 3 is acknowledged. The traversal is on the ground(s) that it would not be a burdensome search to search both the viral vectors of Group I and the methods of expression in Group III. This is not found persuasive because as set forth in the restriction requirement, each group is separate and distinct, separately classifiable, and would require differing strategies for searching. For example the viral vectors can be used to interrupt gene sequences in the target cell, and not for expression of a heterologous sequence.

The requirement is still deemed proper and is therefore made **FINAL**.

Claims 11-17, 24-26 and 32-47 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 3.

Specification

The disclosure is objected to because of the following informalities: The address of the ATCC depository should be amended to reflect the new location (see page 32). The new address for the ATCC is as follows:

American Type Culture Collection
10801 University Boulevard
Manassas, Va 20110-2209

Addtionally, the specification should be amended to recite the ATCC depository numbers in the places left blank at filing (see page 32).

An improper reference is made to a US Application Serial Number (see page 5). This recitation should be replaced with the appropriate US Patent Number (5,753,499).

Appropriate correction is required.

Claim Rejections - 35 USC § 112

Claims 1-10, 18-23 and 27-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the insertion of the particular "ZZ" IgG binding domain of Protein A into a viral vector, does not reasonably provide enablement for insertion of a portion of that domain, or for a portion of any IgG binding domain of Protein A. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims..

The claims are drawn to viral vectors having at least a portion of an IgG binding domain of Protein A.

The specification sets forth the use of the specific, synthetic ZZ domain, which is an IgG binding domain of Protein A from *Staphylococcus aureus*. The entire domain is inserted into the viral envelope. The specification does not disclose what portions of the ZZ domain are necessary and sufficient to retain IgG binding properties, nor does this information appear to be available in the art such that one of skill in the art would be able to identify portions of the ZZ domain which would function as set forth in the specification and claims.

Protein: protein interactions are not strictly predictable such that one can look at the sequences of two proteins and immediately grasp what portions are necessary and sufficient for their interaction. While the skill in the art of virology and protein interactions is high, the identification of portions of polypeptides which would possess the desired properties is unpredictable. The specification does not provide working examples of any fragments or portions of the ZZ domain which would be useful in the invention. While working examples are not required in an application, the specification must provide adequate teachings and guidance such that one of skill in the art would be able to practice the invention.

Additionally, the specification does not disclose that any other IgG binding domain, or portion of any other IgG binding domain of Protein A would be useable in the invention. Protein A is known to have at least 4 IgG binding domains, having varying specificity for immunoglobulin. (see Surolia 1982 Trends Biochem. Sci 7:74-76). Consequently, it would not be clear to one of skill in the art whether any natural IgG binding domain, or portion thereof, would be able to function in the same manner as the synthetic ZZ binding domain disclosed in the specification.

As such, the specification is not enabling for the breadth of the claims.

Claims 1-10,18-23, and 27-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the insertion of synthetic Protein A IgG "ZZ" binding domain into a full length viral protein, does not reasonably provide enablement for fragments of those viral proteins. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims..

The claims recite that the IgG binding domain of Protein A is fused with, or is inserted into the envelope protein or fragment thereof, and that the envelope protein or fragment is capable of directing particle assembly.

The specification, as filed, sets forth the insertion of the ZZ domain of Protein A into the full length envelope protein of Sindbis virus and the replacement of particular sequences in the Mo-MuLV envelope protein with the ZZ domain. The specification does not disclose the use of fragments of the Sindbis virus envelope gene, nor does it describe any other fragments of the Mo-MuLV envelope gene. Applicant does not disclose which portions of those genes are necessary and sufficient to direct particle assembly. The term "fragment" can encompass peptides as small as one amino acid, but such fragments are not described in the specification. Applicant fails to identify the regions of the viral envelope genes necessary to direct particle assembly, nor is it clear that one of skill in the art would readily be able to identify such regions. Applicant provides no guidance as to how one of skill in the art could identify such fragments of

the viral envelope proteins that could direct particle assembly. While working examples are not required in the specification, the specification must provide appropriate teachings and guidance such that one of skill in the art could practice the invention as claimed.

Claims 3-5, 9, and 18-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 is rendered vague and indefinite by the use of the phrase "the vector further comprises a portion of the gp70." It is unclear what Applicant is claiming. Is this gp70 in addition to the viral envelope protein recited in claims 1 and 2? Or is the viral envelope protein recited in the independent claim intended to be the gp70? It would appear from claims 4 and 5 that Applicant intends the latter, but the claim, as written, is not so limited.

Claim 9 recites the limitation "the chimeric gene" in reference to claim 8. There is insufficient antecedent basis for this limitation in the claim. Neither claim 8, nor the claims from which it depends, recites "a chimeric gene".

Claims 18-23 are rendered vague and indefinite by the use of the term "viral complex" The claims do not recite a virus such that a viral complex can result. The claim merely recites a protein and a gene of interest. These components do not form viral complexes.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-10, 18-23, and 27-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barber et al. (US Patent 5,591,624) and Wickham et al. (US Patent 5,846,782), in view of Nilsson et al. (Nilsson et al. 1987 Protein Eng. 1: 107-113)

Claims 1-10 are drawn to viral vectors having an IgG binding domain fusred with, or inserted into a viral envelope gene. Gp70 of Mo-MuLV and E2 of Sindbis are preferred envelope genes. Claims 18-23 are drawn to viral complexes comprising the chimeric envelope protein and a gene of interest. Claims 27-31 are drawn to packaging cell lines comprising the vectors, and heterologous genes of interest.

Barber et al. disclose that viral surface proteins can be altered to redirect their specificity.

At column 20, lines 64-65, Barber et al specifically disclose that the envelope protein of retroviruses (particularly the gp70 of Mo-MuLV) can be modified to comprise a sequence which would bind to the Fc portion of an antibody. The synthetic ZZ IgG binding domain sequences of Protein A disclosed by Nilsson et al. is such a binding sequence. This modification of the envelope genes is done to alter the viral tropism and to facilitate infection of particular cell types, which then mediates gene transfer. Monoclonal antibodies are bound to the IgG binding domain on the viral surface, then the viral complex can be used to infect cell types which react with the particularly selected monoclonal antibody. The virus can carry genes encoding various heterologous sequences, such as drug resistance or sensitivity genes, or genes encoding cell cycle proteins.

Wickham et al. disclose various viral vectors which have modified surface proteins such that particular cell types can be targeted. Wickham et al. identifies suitable viral vectors, including retroviruses, and alphaviruses (see column 12). Both Sindbis and Mo-MuLV are specifically recited as desirable vectors. Wickham discloses a list of heterologous genes of interest which may be part of a viral complex (see column 14, line 37 to column 15, line 10).

Taken together, the instant invention appears to be the same or slightly different from the prior art of altering viral vector tropism through modification of the envelope sequence.

One of ordinary skill in the art at the time the invention was made would have been motivated to select and evaluate the use of the IgG binding domain of Protein A, as it binds to monoclonal antibodies. Barber et al. disclosed that being able to bind particular monoclonal antibodies to an Fc binding region on a viral complex would provide directed targeting for gene

transfer. Both Barber et al. and Wickham et al. disclose viral vectors suitable for such modifications, as well as heterologous genes for gene transfer. Nilsson et al. provide the synthetic IgG binding domain. Based on the aforementioned disclosures it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A Zeman whose telephone number is (703) 308-7991. The examiner can be reached between the hours of 7:30 am and 5:00 pm Monday through Thursday, and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner=s supervisor, Anthony Caputa, can be reached at (703) 308 3995.

The fax number for this Art Unit is (703) 305-7401.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert A. Zeman
April 6, 2000

DONNA WORTMAN
PRIMARY EXAMINER